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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,282	06/27/2007	Michele Reboud-Ravaux	045636-5084	2668

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MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,282	REBOUD-RAVAUX ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-22,24,25 and 28-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *19-22,24,25,28,30,31,34-39,44 and 45* is/are allowed.

6)☒ Claim(s) *29,32,33 and 40-42* is/are rejected.

7)☒ Claim(s) *43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 23, 26 and 27 have been canceled. Claims 19, 22, 29, 35, 43 have been amended. Claims 19-22, 24, 25 and 28-45 are pending and under consideration.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29, 40 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "Ava" and "Bpa" in claim 29 (bottom of page 7) lacks specific antecedent basis within the claim.

Claims 40 and 41 are vague and indefinite due to dependency upon canceled claims 26 and 27.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32, 33 and 42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating diseases or conditions taught in the prior art as being treatable by inhibitors of proteosome activity, does not reasonably provide enablement for methods of preventing said diseases before they occur in an individual, or methods of treating diseases or conditions not recognized to be modulated by proteasome activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re wands, 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(A) As drawn to prevention

Claim 32 and 33 are broadly drawn to the prevention of various diseases and disorder which include cancer, autoimmune disease, AIDS, inflammatory disease, cerebral, pulmonary and myocardial ischemic pathologies, as well as amyotrophy, stroke, traumas, burns and pathologies associated with aging. Claim 42 specifies that a human is administered the molecule of claim 19.

When given the broadest reasonably interpretation, "preventing" one of the aforesaid diseases or conditions includes preventing said disease or condition in an individual who has as yet never been afflicted with said disease or conditions, and thus must entail the administration of the compound of claim 19 before said disease or condition occurs. In order to carry out this method of prevention it would be necessary to identify individuals who will develop the disease or condition before it occurs in said individuals, and to administer the compounds of claim 19 to said individual before onset of the disease. The specification fails to teach how to identify individuals who will develop cancer, autoimmune disease, AIDS, inflammatory disease, cerebral, pulmonary and myocardial ischemic pathologies, amyotrophy, stroke, traumas, burns, Alzheimer's disease or Parkinson's disease. The specification fails to teach the time point for administering the compound of claim 19 to said individuals before the disease occurs, or the length of time for continuing the administration. It is further noted that AIDS is an infection disease, and in order to "prevent" AIDS, infection must not occur. The specification fails to support the notion that administration of a compound which can modulate the proteasome can prevent and infection by a virus. Further, claim 33 encompasses the prevention of "burns" and "trauma". When given the broadest reasonable interpretation, trauma includes injuries sustained in a accident such as an automobile accident or gun shot wound as well as psychological injury. There is no basis in the specification to provide a notion that trauma and burns can be prevented

by administration of the compounds of claim 19. Given the lack of guidance in the specification, one of skill in the art would be subject to undue experimentation without reasonably expectation of success in order to carry out the method of disease prevention by administration of the compounds of claim 19.

(B)As drawn to the treatment of cardiac, cerebral and pulmonary ischemia, cerebra; stroke, traumas and burns.

The prior art teaches that impairment of the proteasome contributes to Parkinson's Disease (Shamoto-Nagai et al, Journal of Neural Transmission, 2004, Vol. 111, pp. 1253-1265), Alzheimer's disease (Song and Jung, Trends in Molecular Medicine, 2004, vol. 10, pp. 565-570) and that inhibition of the proteasome can reduce the severity of psoriasis (Zollner et al, Journal of clinical Investigation, 2002, Vol. 109, pp. 671-679) and arthritis (Firestein, Arthritis and Rheumatism, 2004, Vol. 50, pp. 2381-2386), although there are concerns about the toxicity associated with a general inhibition of proteasome activity (Firestein, ibis, page 2384, first column, first full paragraph). The prior art suggests that protesome inhibitors can be used to inhibit the release of HIV from an infected cell (Schbert et al, PNAS, 2000, vol. 97, pp. 13057-13062). The prior art teaches the administration of proteasome inhibitors for the treatment of various cancers (Adams et al, Investigational New Drugs, 2000, vol. 18, pp. 109-121 and Lightcap et al, Clinical chemistry, 2000, vol. 46, pp. 673-683). The prior art suggests that proteasome inhibitors can be used to treat muscle wasting, and the prevention of transplant rejection (Reboud-Ravaux, Progress in Molecular and subcellular Biology, 2002, vol. 29, pp. 109-125, IDs reference, see page 119) and therefore it would be reasonable to conclude that proteasome inhibitors can be used to treat amyotrophy and allograft rejection. the prior art teaches that proteasome inhibitors can be used to treat inflammation and asthma (Takaoka et al, Current Vascular Pharmacology, 2003, vol. 1, pp. 19-26, see page 19, column 2, lines 2-4).

The prior art teaches that pre-treatment with proteasome inhibitors can reduce the severity of injury in animal models of heart and brain ischemia (Kukan, Journal of Physiology and Pharmacology, 2004, Vol. 55, pp. 3-15). However, there is no evidence that administration of proteasome inhibitors can treat the ischemia-associated injury after it occurs .

Claim 33 is broadly drawn to encompass traumas, burns and pathologies associated with aging beyond those of Alzheimer's and Parkinson's diseases and chorological skin again and

skin photo aging. There is no guidance in the specification for how to provide the compounds of claim 19 for the generic treatment of "pathological associated with ageing". It is noted that administration of proteasome modulators are associated with toxicity because of the immense number of proteins affected by the proteasome (Firestein, ibis, page 2384, first column, first full paragraph). There is no guidance given in the specification for how to treat generic pathologies associated with aging by the administration of a compound of claim 19 which would minimize the toxic effects of the modulators. Further, when given the broadest reasonable interpretation, trauma includes injuries sustained in a accident such as an automobile accident or gun shot wound and psychological trauma. There is no guidance in the specification or any art of record to indicate that the modulators of claim 19 can be used to treat trauma and burns once occurred. One of skill in the art would be subject to undue experimentation in order to carry out the broadly claimed methods.

Claims 29, 32, 33 and 40-42 are rejected.

Claim 43objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 19-22, 24, 25 and 28, 30, 31, 34-39, 44 and 45 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A Canella/
Primary Examiner, Art Unit 1643